UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,480	07/31/2006	Marc Gerspacher	33587-US-PCT	5896

75074 7590 02/16/2011

NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH, INC.
220 MASSACHUSETTS AVENUE
CAMBRIDGE, MA 02139

EXAMINER	
BASQUILL, SEAN M	

ART UNIT	PAPER NUMBER
1613	

NOTIFICATION DATE	DELIVERY MODE
02/16/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

NIBR.MAILDATA@NOVARTIS.COM
PATRICIA.HOFSTETTER@NOVARTIS.COM

Office Action Summary	Application No.	Applicant(s)	
	10/585,480	GERSPACHER ET AL.	
	Examiner	Art Unit	
	Sean Basquill	1613	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1, 2, and 4 have been amended, and Claims 7-11 cancelled. Claims 1-6 are presented for examination.

Previous Rejections

2. Applicants' arguments, filed 3 December 2010, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112 First Paragraph

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 1-3, 5, and 6 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants arguments have been fully considered and are deemed unpersuasive. As the examiner indicated in the previous office action, the scope of compounds claimed far exceeds the

scope of compounds applicants have demonstrated, by the examples provided, that they were in possession of as the skilled artisan would understand the disclosure as originally filed. To be sure, the breadth of claim scope to which applicants are entitled is not exclusively limited by the examples that applicants particularly and specifically describe. However, it is with these specific examples that the analysis begins. The skilled artisan would be well aware that the possession of chemical compounds bearing certain chemical moieties would reasonably convey to the skilled artisan that equivalent moieties were in the applicants possession as well. Alkyl chain homologs and certain heteroatom substitutions, for example, are well-known and commonly employed examples of bioisosteric equivalents well within the ability and cognizance of the skilled artisan. See, e.g., George Patani & Edmond LaVoie, Bioisosterism: A Rational Approach in Drug Design, 96 CHEM. REV. 3147 (1996) (describing the concept of bioisosterism and the substitution of halogens for hydrogen and methyl groups, the substitution of one heteroatom selected from the groups of O, N, and S, each for the other, are commonly employed by medicinal chemists in modifying lead compounds to alter pharmacokinetic and other pharmacological properties). This is of particular importance concerning the applicants claims directed to substituents on the 3(N)- and 4- positions on the benzimidazole ring. Applicants have only provided evidence that either lower alkoxy or halo substituents are present as an N substituent, which would convey to the skilled medicinal chemist the possession of lower alkyl, halo, lower alkoxy, lower thioxy, and lower amino substituents. In a similar manner, substituents on the 4- position of the benzimidazole ring (substituent R6) are limited to methoxy, thiomethyl, dimethylamino ethyl, and lower alkyl moieties.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 1-6 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 6,855,714 ("Blume"), in view of George Patani & Edmond LaVoie, Bioisosterism: A Rational Approach in Drug Design, 96 CHEM. REV. 3147 (1996) ("Patani").

Applicants arguments have been fully considered and are deemed unpersuasive. Applicants have argued that because the Compounds of Blume are disclosed as microglial activators, opposed to the parathyroid hormone release stimulators applicants have characterized the compounds of the instant invention, that the necessary second prong of the In re Wilder analysis, namely commonality of utility, is not present, and the compounds claimed cannot be rendered obvious as a result. Applicants rebuttal misconstrues the scope of the invention they have claimed and therefore misapplies the holding of In re Wilder, and cannot overcome the examiner's prima facie case of obviousness on the basis of the record at present.

Applicants claims are directed to compounds having a phenyl-benzimidazole core. Applicants have characterized these compounds as possessing the ability to stimulate the release of parathyroid hormone. Applicants are indeed correct that the compounds disclosed by Blume are characterized as possessing the ability to inhibit microglial activation, but their argument that such distinction in characterized properties renders the application of In re Wilder inapplicable to the instant Claims is itself improper. Applicants claims, directed to the compounds rather than any particular application thereof, if granted would preclude any and all use of compounds falling within the four corners of the genus they have described. While it is true that the

applicants have indicated the desire to stimulate parathyroid hormone release motivated the inventors to arrive at the instantly claimed compounds, the examiner is not bound by the same rationale in arriving at a prima facie case of obviousness. See MPEP 2144 (indicating that employing a rationale different from that utilized by the applicants is permissible in formulating a prima facie case of obviousness). Here, Blume discloses a genus of phenyl-benzimidazole derivative compounds substantially similar to the instant compounds of Formula I, particularly compounds 32, 36, 4, 55, 58, 74, 84, and 86 described in Table 1. Each of these possesses an R1, R2, R4, R5, and R7 substitution falling within the genus of compounds claimed. The only distinction between the compounds specifically listed above and the compounds claims can be found in positions R3 and R6 of the instant claims, where the compounds of Formula I carry, for example Halo substitutions and the compounds of Blume carry hydrogen substitutions. Looking to the disclosure of Patani, discussed in greater detail in the previous office action, medicinal chemists are well aware of the concept of bioisosterism and commonly employ the introduction of bioisosteric equivalent functional groups to alter the pharmacological properties of known compounds. It is within this context, modifying the known microglial inhibitors of Blume to form additional, structurally related and bioisosterically equivalent microglial inhibitors, that the holding of In re Wilder is applied.

Applicants have claimed chemical compounds; whatever rationale the examiner applies, references which render those compounds obvious may properly form the basis of a prima facie case. Blume discloses related phenyl-benzimidazole compounds which are known to inhibit microglia. The skilled medicinal chemist looking to the disclosures of Blume and Patani would recognize that the bioisosteric substitution of fluorine for hydrogen in the Blume compounds

would result in compounds also possessing microglial inhibitory activity with different pharmacological properties. Under the reasoning of In re Wilder, then, such a modification would be expected to result in compounds not only structurally similar but which possess a common utility; to properly rebut the examiner's prima facie case within this context, applicants must demonstrate that the Blume compounds modified in such a manner do not retain this microglial inhibitory activity.

Unless and until applicants properly present evidence either rebutting the examiner's case or which demonstrates appropriate secondary indicia of nonobviousness, the above rejection shall stand.

Conclusion

No Claims stand allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean Basquill whose telephone number is (571) 270-5862. The examiner can normally be reached on Monday through Thursday, between 8AM and 6PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Kwon can be reached on (571) 272-0581. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sean Basquill/
Examiner, Art Unit 1613

/Jeffrey S. Lundgren/
Primary Examiner, Art Unit 1639